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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/557,907	04/21/2000	Holly Horton	1530.0060004/EKS/EJH	9397

26111 7590 11/07/2005

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/557,907	HORTON ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,16-18,30-35,38-41,43,46-50,66,69,71-74,77,78 and 83-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, 16-18, 30-35, 38-41, 43, 46-50, 66, 69, 71-74, 77, 78 and 83-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-7, 16-18, 30-35, 38-41, 43, 46-50, 66, 69, 71-74, 77, 78 and 83-86 remain pending and under consideration in the instant office action.

Applicant's arguments filed 8-24-05 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-7, 16-18, 30-35, 38-41, 43, 46-50, 66, 69, 71-74, 77, 78 and 83-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "mammal in need of cancer treatment" in claim 1, 66 and 78 is new matter. Pg 104, lines 9-22, cited by applicants for support, is limited to mammals having cancer. The scope of "mammal in need of cancer treatment" is broader than the

disclosure on pg 104, lines 9-22, as it encompasses treating mammals at risk for cancer which was not originally disclosed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-7, 16-18, 30-35, 38-41, 43, 46-50, 66, 69, 71-74, 77, 78 and 83-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "mammal in need of cancer treatment" in claims 1, 66 and 78 is indefinite. It is unclear if the phrase is limited to a mammal having cancer or if the phrase is intended to encompass a mammal at risk for developing cancer and a lab mammal that is about to be given a tumor. For example, a lab mammal may be given the plasmid encoding IFNα before given the tumor to determine whether IFNα expression is capable of inhibiting tumor growth. A lab mammal may also be given a "cancer treatment" without being given cancer. It is unclear if such mammals are encompassed by the claim.

Claim 1 is indefinite because it is unclear if the phrase "said cancer" in the last line refers to the phrase "treating cancer" or the phrase "in need of cancer treatment."

Claim 1, overall, is indefinite because there is no nexus regarding the cancer or the treatment, i.e. the claim does not clearly set forth that the mammal has cancer, that

the level of IFNα expression obtained is capable of treating said cancer, or that said cancer is treated.

Claims 4-6 and 30-34 are indefinite because claims limit the type of "cancer" in claim 1; however, the mammal of claim 1 does not necessarily have cancer. In addition, it is unclear if "said cancer" in claim 4, for example, refers to the phrase "treating cancer or metastasis thereof in a mammal" in the preamble of claim 1 or the phrase "mammal in need of cancer treatment" in the body of claim 1.

Claim 66 and 78, overall, are indefinite because there is no nexus regarding the cancer or the treatment, i.e. the claims do not clearly set forth the steps required to perform the method, i.e. administering the plasmid to a mammal having a tumor or delivering IFNα to the tumor in an amount that inhibits tumor growth.

The phrase "said mammal in need of cancer treatment" in claims 66 and 78 lacks antecedent basis.

Claim Rejections - 35 USC § 102

Claims 1, 3-7, 30-35, 38 and 43 remain rejected under 35 U.S.C. 102(a) as being anticipated by Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261).

Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter in saline into the skeletal tibialis anterior muscle of mice. The injection resulted in physiologically significant amounts of IFN-α in the

systemic circulation (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26).

Without evidence to the contrary, the serum levels obtained by Lawson (22 and 36 IU/ml) are inherently "an amount effective to treat said cancer" as claimed (see pg 259, Table 4).

The phrase "treating cancer or metastasis thereof in a mammal" in the preamble of the independent claims is an intended use and does not bear patentable weight in considering the art because it does not have to occur.

The limitation of expressing IFNα "in the blood stream of said mammal in an amount effective to treat cancer" in the body of claim 1 is equivalent to obtaining serum levels of 22 and 36 IU/ml of INF-α as taught by Lawson. Without evidence to the contrary, the amount of expression obtained by Lawson is inherently is an amount "effective to treat cancer" as claimed. The body of claim 1 does not require a step of inhibiting tumor growth.

The mouse of Lawson (without a tumor) is a "mammal in need of cancer treatment" because it is a mouse receiving a "cancer treatment" (see 112/2nd). The phrase does not clearly set forth that the mammal has cancer.

Assuming *arguendo* the phrase "mammal in need of cancer treatment" is limited to a mammal having cancer, the last two sentences of Lawson state: "[t]he surprisingly simple technique of gene transfer via intramuscular injection of naked DNA allows further investigation of the relative in vivo efficacies of the functional capabilities of each type I IFN subtype in animal models. We are currently systematically analyzing

antitumor and antiviral actions of the murine IFNs in established animal models of disease." It is readily apparent from the last two sentences that Lawson applied the method of administering naked plasmid DNA encoding IFNs intramuscularly to established tumor models, i.e. mammals having tumors, which is equivalent to "a mammal in need of cancer treatment" in the body of claim 1 and "treating cancer" as in the preamble of claim 1.

The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Dependent claims 4-6 and 30-34 are included because the claims limit the type of "cancer" in claim 1; however, the mammal of claim 1 does not necessarily have cancer (see 112/2nd). In addition, it is unclear if "said cancer" in claim 4, for example, refers to the phrase "treating cancer or metastasis thereof in a mammal" in the preamble of claim 1 or the phrase "mammal in need of cancer treatment" in the body of claim 1.

Claim Rejections - 35 USC § 103

Claims 1, 3, 4, 7, 30, 31, 35, 38, 43 and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261) in view of Zhang of record (PNAS, April 1996, Vol. 93, pg 4513-4518).

Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter in saline into the skeletal tibialis anterior muscle of mice. The injection resulted in physiologically significant amounts of IFN-α in the systemic circulation (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26).

Without evidence to the contrary, the serum levels obtained by Lawson (22 and 36 IU/ml) are inherently "an amount effective to treat said cancer" as claimed (see pg 259, Table 4).

The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Lawson did not administer the plasmid to a mouse with breast or melanoma cancer.

However, Zhang established breast or melanoma tumors in the breast or thigh of mice then injected a vector encoding INF into the mice three times resulting in tumor regression.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into the muscle of a mouse as taught by Lawson, wherein the mouse had an established breast or melanoma tumor as described by Zhang. One or ordinary skill in the art at the time the invention was made would have been motivated to use the technique described by Lawson in the mice with tumors described by Zhang because Lawson suggested using the technique in disease

models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence).

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a vector encoding INF into a mouse with a tumor three times as taught by Zhang, wherein the vector was a plasmid encoding INF-α and was injected intramuscularly as described by Zhang. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the viral vector encoding IFN-consensus of Zhang with the plasmid encoding IFN-α described by Lawson to avoid the pathogenicity of adenoviruses (pg 4513, col. 1, last line, of Zhang) and because Lawson suggested using the plasmid in disease models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence).

One of ordinary skill in the art at the time of filing would have had a reasonable expectation of successfully treating tumors in the mice described by Zhang using the technique of Lawson because the serum levels of IFN-α described by Lawson (22 and 36 IU/ml) were capable of treating cancer (see pg 259, Table 4). The serum levels described by Lawson indicate systemic delivery of INF-α, which would ultimately allow contact of INF-α with the tumor through the vasculature.

Claims 46-49 are included because injecting the vector three times as taught by Zhang is equivalent to injecting the plasmid before, during or after gene therapy, i.e. the first injection is followed by gene therapy (the second and third injections), the second injection is preceded and followed by gene therapy (the first and third injection, etc.)

Applicants arguments summarize the teachings of Lawson and Zhang (pg 11, last 6 lines) and conclude that Lawson in view of Zhang do not teach all the limitations of claims. Applicants' arguments are not persuasive because applicants have not pointed to one specific element that the combined teachings of Lawson and Zhang fail to teach.

Applicants argue that one of ordinary skill would not have been motivated to combine Lawson and Zhang because Lawson taught away from Zhang. Applicants assert that one of skill would not have been motivated to cause a crush injury in order to treat cancer. Applicants' argument is not persuasive. Applicants' assertion is unfounded. One of ordinary skill would have done most anything to a lab mouse as evidenced by Lawson who crush injured the muscle of a mouse that did not have disease. One of ordinary skill would have crush injured the muscle of a mouse with a tumor to prevent the death of the mouse; crushing the muscle of the mouse is better than having the mouse die. Furthermore, Lawson specifically suggested administration of naked plasmid encoding IFNs via intramuscular injection to established tumor models (last two sentences of Lawson).

Claims 1, 3, 7, 35, 38 and 43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ogura (Cancer research, 1990 Aug 15, Vol. 50 (16) pg 5102-6) in view of Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261).

For this rejection, claim 1 is being interpreted as though the DNA plasmid was injected into a mammal having cancer or metastasis thereof.

Ogura established tumors in mice then injected a chamber apparatus subcutaneously, wherein the chamber apparatus comprised fibroblasts transfected with a plasmid encoding INF-α into the tumors resulting in tumor regression (pg 5103, last full ¶). The tumors were made using the chronic myelocytic leukemia cell line, KU812 (pg 5102, last 4 lines). Ogura did not inject the vector intramuscularly in the absence of the fibroblasts.

However, Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter in saline into the skeletal tibialis anterior muscle of mice. The injection resulted in physiologically significant amounts of IFN-α in the systemic circulation (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26). The serum levels obtained by Lawson (22 and 36 IU/ml) are effective to treat cancer (pg 259, Table 4). The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into the mouse with a tumor as taught by Ogura, wherein the plasmid was in the absence of cells and injected intramuscularly as described by Lawson. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the cells transfected with a plasmid encoding IFN-α described by Ogura with plasmids encoding IFN-α described by

Lawson to avoid the steps of transfecting cells with the plasmid and culturing the cells in vitro.

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into a mouse intramuscularly as taught by Lawson, wherein the mice had established myelocytic leukemia tumors as described by Ogura. One or ordinary skill in the art at the time the invention was made would have been motivated to perform the technique of Lawson in the mice described by Ogura because Lawson suggested using the plasmid in disease models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence).

One of ordinary skill in the art at the time of filing would have had a reasonable expectation of successfully treating tumors in the mice described by Ogura using the technique of Lawson because the serum levels of IFN-α described by Lawson (22 and 36 IU/ml) were capable of treating cancer (see pg 259, Table 4). The serum levels indicate systemic delivery of INF-α, which would ultimately allow contact of INF-α with the tumor through the vasculature.

Applicants arguments summarize the teachings of Ogura and Lawson (pg 12, last 7 lines) and conclude that Ogura in view of Lawson do not teach all the limitations of claims. Applicants' arguments are not persuasive because applicants have not pointed to one specific element that the combined teachings of Lawson and Ogura fail to teach.

Applicants argue that one of ordinary skill would not have been motivated to combine Lawson and Ogura because Lawson taught away from Ogura. Applicants

assert that one of skill would not have been motivated to cause a crush injury in order to treat cancer. Applicants' argument is not persuasive. Applicants' assertion is unfounded. One of ordinary skill would have done most anything to a lab mouse as evidenced by Lawson who crush injured the muscle of a mouse that did not have disease. One of ordinary skill would have crush injured the muscle of a mouse with a tumor to prevent the death of the mouse; crushing the muscle of the mouse is better than having the mouse die. Furthermore, Lawson specifically suggested administration of naked plasmid encoding IFNs via intramuscular injection to established tumor models (last two sentences of Lawson). Ogura is one such tumor model.

Claims 66, 69, 71-73 78 and 83-85 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki (Human gene therapy, 1997 Jun 10, Vol. 8 (9) pg 1105-13) in view of Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261) and Welander (Investigational New drugs, 1987, Vol. 5, Suppl, S47-59, abstract only).

Aoki established pancreatic tumors in the peritoneal cavity of mice then injected a plasmid encoding HSV-TK operably linked to a promoter in a cationic liposome into the peritoneal cavity of the mice resulting in tumor regression. Aoki did not inject a vector encoding IFN-α.

However, Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter into mice resulting in IFN-α expression (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Persistence of IFN expression in muscle," "Circulating IFN protein levels in serum"; see also the

specification on pg 4, lines 24-26). The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding a protein capable of treating cancer in a cationic liposome into the peritoneal cavity of a mouse with a peritoneal tumor as taught by Aoki, wherein the plasmid encoded IFN-α as described by Lawson. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the plasmid encoding HSV-TK described by Aoki with the plasmid encoding IFN-α described by Lawson to avoid the use of the suicide gene HSV-TK and because intraperitoneal injection of INF-α was known to have anti-tumor effect (Welander abstract, last 5 lines).

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into a mouse as taught by Lawson, wherein the mice had established tumors as described by Aoki. One or ordinary skill in the art at the time the invention was made would have been motivated to use the plasmid of Lawson mice with established peritoneal tumors as described by Aoki because Lawson suggested using the plasmid in established disease models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence). One of ordinary skill would have been motivated to inject the plasmid encoding INF-α described by Lawson intraperitoneally as described by Aoki to maximize the level of INF-α and the tumor cell exposure to INF-α as described by Welander.

Applicants' arguments summarize the teachings of Aoki, Lawson and Welander (pg 13, last 8 lines) and conclude that the combined teachings of Aoki, Lawson and Welander do not teach all the limitations of claims. Applicants' argument is not persuasive because applicants have not pointed to one specific element that the combined teachings of Aoki, Lawson and Welander fail to teach.

Applicants argue that one of ordinary skill would not have been motivated to combine Aoki, Lawson and Welander because Lawson taught away from the combination. Applicants assert that one of skill would not have been motivated to cause a crush injury as taught by Lawson in order to treat cancer as taught by Aoki. Applicants' argument is not persuasive. First, applicants' assertion is unfounded. Second, one of ordinary skill would have done most anything to a lab mouse as evidenced by Lawson who crush injured the muscle of a mouse that did not have disease. If one of ordinary skill would have crush injured the muscle of a normal mouse as taught by Lawson, one of ordinary skill would not have any qualms about crush injuring the mouse with a tumor taught by Aoki to prevent the death of the mouse; crushing the muscle of the mouse is better than having the mouse die. Furthermore, Lawson specifically suggested administration of naked plasmid encoding IFNs via intramuscular injection to established tumor models (last two sentences of Lawson). Aoki is clearly an art established tumor model.

Claims 1, 3-7, 30-35, 39-41, 43 and 46-49 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Okamoto (Gene Therapy, 1997, Vol. 4, pg 969-976) in view of Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261).

Okamoto injected a plasmid encoding a protein operably linked to a promoter in a cationic liposome into the quadricep of mice (Fig. 1). The mice were immunized three times (pg 971, Fig. 2 caption). Okamoto did not inject a vector encoding IFN-α.

However, Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter intramuscularly into mice resulting in IFN-α expression (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Persistence of IFN expression in muscle;" see also the specification on pg 4, lines 24-26).

The mouse of Lawson (without a tumor) is a "mammal in need of cancer treatment" because it is a mouse receiving a "cancer treatment." The phrase does not clearly set forth that the mammals have cancer or that cancer treatment occurs.

The limitation of expressing IFNα "in the blood stream of said mammal in an amount effective to treat cancer" in the body of claim 1 is equivalent to obtaining serum levels of 22 and 36 IU/ml of INF-α as taught by Lawson. Without evidence to the contrary, the amount of expression obtained by Lawson is inherently is an amount "effective to treat cancer" as claimed. The body of claim 1 does not clearly set forth that any specific anti-tumor "treatment" occurs that is distinguished over Lawson.

The phrase "of treating cancer or metastasis thereof in a mammal" in the preamble of claim 1 is an intended use and does not bear patentable weight in

considering the art because the body of the claim does clearly set forth the mammal has cancer or that cancer treatment occurs.

The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding a protein in a liposome intramuscularly into a mouse as taught by Okamoto, wherein the plasmid encoded IFN-α as described by Lawson. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the plasmid encoding MAGE-3 taught by Okamoto with the plasmid encoding IFN-α described by Lawson to determine the immune response to IFN-α in vivo. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into a mouse intramuscularly as taught by Lawson using an HVJ-liposome as described by Okamoto. One or ordinary skill in the art at the time the invention was made would have been motivated to add the HVJ-liposome described by Okamoto to the plasmid of Lawson because Okamoto taught HVJ-liposomes caused expression of the protein but plasmid alone did not (see abstract). One of ordinary skill in the art at the time the invention was made would have been motivated to use the plasmid of Lawson in the method of Okamoto because Lawson suggested using the plasmid in established models (pg 256, col. 1, lines 12-14).

Dependent claims 4-6 and 30-34 have been included because they further limit the phrase in the preamble and do not bear patentable weight.

Claims 46-49 are included because injecting the vector three times is equivalent to injecting the plasmid before, during or after gene therapy, i.e. the first injection is followed by gene therapy (the second and third injections), the second injection is preceded and followed by gene therapy (the first and third injection, etc.

Applicants' arguments summarize the teachings of Okamoto and Lawson (pg 14, last 5 lines and pg 15, first two lines) and conclude that the combined teachings of Okamoto and Lawson fail to teach all the limitations of claims. Applicants' argument is not persuasive because applicants have not pointed to one specific element that the combined teachings of Okamoto and Lawson fail to teach.

Applicants argue that one of ordinary skill would not have been motivated to combine Okamoto and Lawson because Lawson taught away from the combination. Applicants assert that one of skill would not have been motivated to cause a crush injury in order to treat cancer. Applicants' argument is not persuasive. Applicants' assertion is unfounded. One of ordinary skill would have done most anything to a lab mouse as evidenced by Lawson who crush injured the muscle of a mouse that did not have disease. If one of ordinary skill would have crush injured the muscle of a normal mouse, one of ordinary skill would not have any qualms about crush injuring the muscle of other normal mice as described by Okamoto.

Double Patenting

The rejection of claims 1, 3, 4, 16, 17, 30-32, 35, 38-41, 43 and 46-49 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 30, 31, 34, 35 38-44, 47, 48, 49, 51 and 52 of U.S. Patent No. 6,875,748 in view of the disclosure of '748 has been withdrawn in view of the terminal disclaimer filed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Horton (PNAS, Feb. 1999, Vol. 96, pg 1553-1558).

Manthorpe cited above under the obviousness type double patenting rejection (US Patent 6,875,748; Application No: 09/839,574, filed 4-23-01 and having priority to 11-28-00) was not available as prior art at the time the invention claimed in the instant application was made. The claimed invention in the instant application was at least taught in parent application 09/196,313, filed 11-20-98 to which applicants claim priority (see for example pg 59). Therefore, Manthorpe (effective filing date = 11-28-00) was not available as prior art at the time the invention claimed in the instant application was made (effective filing date is at least 11-20-98).

Wolff (US Patent 6,228,844) claims a method for stimulating vascular growth in the heart of a vertebrate, comprising injecting into the myocardium of the vertebrate a noninfectious, nonintegrating DNA construct comprising a promoter operably linked to a DNA sequence encoding vascular endothelial growth factor; wherein said DNA

construct is injected in an amount sufficient that uptake of said DNA construct into cardiac cells of the vertebrate occurs, and sufficient expression of said vascular endothelial growth factor results, to stimulate vascular growth; and wherein said DNA construct is free from association with transfection-facilitating proteins, viral particles, liposomal formulations, charged lipids, and calcium phosphate precipitating agents. '844 suggested delivering interferons using DNA and delivering DNA to treat cancer. '844 did not teach IFN-α or obtaining expression levels of a protein in the serum that were capable of treating cancer by administering the DNA intramuscularly or into the peritoneal cavity as currently claimed.

Wolff (US Patent 6,706,694; Application No: 09/588,655) claims a method for delivering a physiologically active polypeptide to a vertebrate heart, comprising: administering in vivo into heart muscle of a vertebrate a composition comprising a DNA operably encoding said physiologically active polypeptide through association with a promoter which directs synthesis of said polypeptide in vertebrate heart cells, and a pharmaceutically acceptable carrier; wherein said polynucleotide is free from association with liposomal formulations, charged lipids, transfection-facilitating precipitating agents, and transfection-facilitating viral particles; wherein a sufficient amount of said composition is administered to allow incorporation of said polynucleotide into heart cells of said vertebrate; and wherein said polypeptide is expressed in the heart of said vertebrate. '694 suggested delivering interferons using DNA and delivering DNA to treat cancer. '694 did not teach IFN-α or obtaining expression levels of a protein in the serum that were capable of treating cancer by administering the DNA

intramuscularly or into the peritoneal cavity as currently claimed. It is not readily apparent that administering polynucleotides to the heart as in '694 can be used to treat cancer or metastasis as claimed in the instant application.

US Application number 10/028,782 has been considered for potential double patenting; however, '782 is limited to administering RNA which is patentably distinct from administering a DNA plasmid as claimed in the instant invention.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER